Complete Summary

GUIDELINE TITLE

Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb. 29 p. (Technology appraisal guidance; no. 137).

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Health and Clinical Excellence (NICE). Guidance on the use of rituximab for recurrent or refractory Stage III or IV follicular non-Hodgkin's lymphoma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2002 Mar. 24 p. (Technology appraisal guidance; no. 37).

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- September 11, 2008, Rituxan (Rituximab): Genentech informed healthcare professionals of revisions to prescribing information for Rituxan regarding a case of progressive multifocal leukoencephalopathy (PML) leading to death in a patient with rheumatoid arthritis who received Rituxan in a long-term safety extension clinical study.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Relapsed stage III and IV follicular non-Hodgkin's lymphoma
- Refractory stage III and IV follicular non-Hodgkin's lymphoma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To review the data available on the clinical and cost effectiveness of rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma

TARGET POPULATION

People in England and Wales with stage III or IV follicular non-Hodgkin's lymphoma

INTERVENTIONS AND PRACTICES CONSIDERED

1. Rituximab monotherapy
2. Rituximab in combination with chemotherapy

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
    - Tumor response rate (partial response and complete response)
    - Duration of response/remission
    - Health-related quality of life
    - Event-free survival

    - Time to new treatment or progression
    - Overall survival
    - Adverse events
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Liverpool Reviews and Implementation Group (see the "Availability of Companion Documents" field).

Clinical Effectiveness Literature Search

Description and Critique of Manufacturers Search Strategy

Seven electronic databases were searched (Medline, Medline in process, Embase, Embase alerts, Biosys, Blood online, The Cochrane Library controlled trials database) covering the period 01/01/2000 to April/May 2007. The manufacturer also reviewed its original European Medicines Evaluation Agency (EMEA) submission for additional relevant information.

All relevant databases were searched and, after clarification from the manufacturer, comprehensive and appropriate search strategies were provided to the ERG in order to make the searches reproducible.

Inclusion/Exclusion Criteria

The inclusion and exclusion criteria used in the study selection were not explicitly stated in the manufacturer's submission (MS). However, a flow diagram of study selection shows reasons for exclusion of articles (Figure 4-1 of the original ERG report [see the "Availability of Companion Documents" field). The manufacturer does not state whether or not the inclusion/exclusion criteria used were predefined or how criteria were applied.

The MS presents 24 references for clinical papers from 5 trials that were examined in stage 2 of the inclusion process. Three of these trials (10 papers) were excluded due to non-licensed indication, no non-rituximab, and inappropriate comparator. In the text there is also reference to a further study that was excluded due to the use of non-licensed rituximab *maintenance* in a non-approved indication.

The ERG is confident that no relevant publicly available studies were excluded from the MS.

Cost-Effectiveness Literature Search

Description and Critique of Manufacturers Search Strategy

The databases used in the electronic searches were identified in the MS as Medline, Medline in process, Embase, Embase alerts, Biosys, NHS Economic Evaluation Database (NHS EED) and Health Economic Evaluation Database (HEED). Blood online was also searched for abstracts. Key search terms were stated but no original search strategy was provided. The term "rituxan" is cited as a key search term; however, it is not clear from the manufacturer's description why the term "MabThera" was not also used. One of the studies in the review has a publication date of 1999, yet the search period stated is 2000 to May 2007. From the results described, it appears that the Wake study (identified as study 5 and study 69 in the MS) has been excluded for two different reasons: NICE document and clinical paper. Finally, the MS did not include an economic evaluation search flow diagram.

The ERG's review of the inclusion and exclusion file in appendix 10 of the MS reveals that from a total of 73 identified studies, nine were included in the review. The ERG concludes that reasons for exclusion are as follows: not indication of interest (n=26); NICE document (n=4); NICE guidance (n=2); clinical (n=21); not disease area of interest (n=4); not treatment of interest (n=2); patients who are refractory to rituximab (n=2); same model as presented in the submission using Canadian costs (n=1); looking at indirect costs (n=2).

Refer to the ERG Report (see the "Availability of Companion Documents" field) for further details of the clinical and cost effectiveness reviews.

NUMBER OF SOURCE DOCUMENTS

- The manufacturer's submission (MS) provides clinical evidence from two randomized controlled trials.
- The MS presents the results of two sets of economic evaluations.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Subjective Review

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by the Liverpool Reviews and Implementation Group (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Clinical Evidence

The two relevant randomized controlled trials (RCTs) were included in the manufacturer's systematic review (SR) are the European Organisation for Research and Treatment of Cancer (EORTC) and German Low grade Lymphoma Study Group-Fludarabine, Cyclophosphamide and Mitoxantrone (GSLG-FCM) trials. Both trials are phase III, multi-centre, randomized, open-label trials designed to evaluate the efficacy and safety of: (i) rituximab in combination with chemotherapy in inducing a remission in follicular non-Hodgkin's lymphoma (FL) and (ii) rituximab as maintenance therapy for FL patients.

Description and Critique of Manufacturers Approach to Validity Assessment

The manufacturer's submission (MS) provides completed validity assessments for the two included trials; no details on who conducted the validity assessment or how it was conducted are detailed. Both trials are considered to be high quality trials although it is noted both were open-label trials and it is unclear from the published papers whether assessors were aware of treatment allocation. The MS also highlights that the GLSG-FCM trial did not use an intention to treat analysis as stated, but rather 19 patients were excluded due to inadequate documentation or were withdrawn between randomisation and delivery of study treatment. Also, analysis of the clinical evidence from the GLSG-FCM maintenance phase is limited as it is unclear how many patients completed the maintenance treatment. The table of validity assessment provided in the MS is included in Appendix 7.2 of the ERG report.

Description and Critique of the Statistical Approach Used in the MS

The MS includes a thorough description of the statistical approaches used in the EORTC trial and the GLSG-FCM trial.

EORTC

The EORTC trial used a chi-square test for trend to examine response rates, with a significance threshold of $P<0.001$, with early stopping allowed if this threshold was crossed. For the secondary endpoints of event-free survival (EFS), overall survival (OS) and the exploratory endpoint progression-free survival (PFS), a log-rank test using a two-sided alpha level of 5% was used. Kaplan-Meier (K-M) curves were produced to graphically display the unadjusted difference between the treatment arms. Results were presented as risk ratios with 95% confidence

intervals (CIs) reported. In the maintenance phase, the primary endpoint of PFS was based on a log-rank test stratified according to induction treatment; secondary and exploratory endpoints were unstratified. For OS in the maintenance phase, an unstratified log-rank test using a two-sided alpha level of 5% was used for the primary analysis and secondary analyses were done by the Cox regression analysis and the results presented as risk ratios including 95% CIs.

The statistical approaches used in trial EORTC are generally appropriate. However, it is unclear as to why a significance threshold of $P<0.001$ was used instead of $P<0.05$ as is usually used when Haybittle-Peto's rule is applied. Furthermore, the trial protocol outlines that secondary analyses in the maintenance phase of the trial will use Cox regression analysis with adjustment for stratification factors and other potential prognostic factors and that the secondary endpoint of OS will be analysed with a log-rank test, stratified for the same factors as PFS. In the MS all analyses of secondary outcomes were unstratified; the reason for this deviation from the protocol is unclear. Finally, EFS results are not reported.

Whilst the EORTC trial allows comparison of the four alternative treatment strategies contained within the trial, as depicted by the 4-arm economic model, the trial was not powered or designed for this specific purpose.

GLSG-FCM

The GLSG-FCM trial used a 1-sided triangular sequential test with a significance level of 0.05, for both the induction and maintenance phases. Exploratory analyses were performed for histological subgroups, the PFS from the start of therapy and OS. The Fisher test was used for analyses of binary responses and the log-rank test and univariate Cox regression for time-censored analyses.

The statistical analyses performed in the GLSG-FCM trial appear to be appropriate. However, only limited results are available for FL patients.

Summary Statement

The SR was adequately conducted by the manufacturer. The two trials included in the SR were of good quality and the primary outcome measures reported in the MS were considered to be appropriate. As specific clinical results for the FL patients in the GLSG-FCM trial were not fully reported in the published papers, the value of the trial results is therefore limited, particularly for patients in the maintenance phase, as they are not focussed on the patient population of interest in this single technology appraisal.

Cost Effectiveness

Critique of Data Extraction and Quality Assessment

The manufacturer presented summary details of the nine studies included in the review in a table which included the following categories: study, aims, methods, results and relevance to decision-making in England and Wales. It is unknown whether or not a second reviewer conducted independent data abstraction or how

any discrepancies were discussed. The manufacturer did not state whether quality assessment of the included studies had been undertaken.

Summary of Cost-Effectiveness Evidence Identified

The manufacturer presented summary details of the nine included studies. The studies were published during the period 1999-2006. Seven of the studies were cost analyses. Only one cost-effectiveness study included rituximab maintenance as a comparator (rituximab maintenance versus autologous stem cell transplant). In a cost-minimisation analysis, the authors assumed that there was no significant difference between the treatments in terms of response rates and disease duration yet went on to describe differences in the incidence and severity of drug-related adverse events. Only two of the nine included studies were conducted in the United Kingdom.

Conclusions

The systematic literature review of the economic evidence conducted by the manufacturer was poor. The ERG concludes that direct or meaningful comparison of the included studies was not possible due to the fact that the economic analyses were very different. In particular, the studies were heterogeneous in terms of the comparators, approaches to costing and country of origin.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The Committee considered the manufacturer's economic model and the critique of it by the Evidence Review Group (ERG). In particular, it discussed the costs included in the model and the approach to survival modelling and extrapolation. The Committee considered the changes to the costs in the manufacturer's model suggested by the ERG. It thought that it was appropriate to calculate costs at progression by aggregating treatments into categories, and it agreed with the ERG's assumptions as to how these would vary across the treatment strategies. It heard from clinical and patient specialists that, although the duration of second and subsequent infusions can sometimes be reduced to as little as 2 hours, for the most part, approximately 4 hours are necessary. The Committee also understood that the practice of rapid administration of rituximab was increasingly followed because its safety was now accepted by clinicians. The Committee concluded that it would currently be more appropriate to cost administration of rituximab as a day-case procedure than as an outpatient visit. The Committee also concurred

with the ERG's approach of adding a terminal-care cost to the model and that the amounts assumed were appropriate. The Committee was not satisfied that the survival modelling adopted by the manufacturer was optimal and regarded the estimates resulting from the manufacturer's initial model as unreliable and requiring further analysis.

See sections 4.7 through 4.12 of the original guideline document for additional discussion of the cost-effectiveness of rituximab.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The Institute reviews each piece of guidance it issues. The review and reappraisal of the use of rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma has resulted in a change in the guidance. In people with relapsed stage III or IV follicular non-Hodgkin's lymphoma, rituximab is now an option in combination with chemotherapy to induce remission or alone as maintenance therapy during remission.

Rituximab monotherapy is also an option for people with relapsed or refractory disease when all alternative treatment options have been exhausted.

Guidance

- Rituximab, within its marketing authorisation, in combination with chemotherapy, is recommended as an option for the induction of remission in people with relapsed stage III or IV follicular non-Hodgkin's lymphoma.
- Rituximab monotherapy as maintenance therapy, within its marketing authorisation, is recommended as an option for the treatment of people with

relapsed stage III or IV follicular non-Hodgkin's lymphoma in remission induced with chemotherapy with or without rituximab.

- Rituximab monotherapy, within its marketing authorisation, is recommended as an option for the treatment of people with relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma, when all alternative treatment options have been exhausted (that is, if there is resistance to or intolerance of chemotherapy).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for the recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate and effective use of rituximab for stage III or IV follicular non-Hodgkin's lymphoma

POTENTIAL HARMS

Allergic and skin reactions are the most common side effects of rituximab infusion. Infusion reactions can be complicated by bronchospasm and hypotension and can occasionally be severe or life threatening. Severe reactions are more common in patients with a high tumour burden, and the incidence and severity of infusion reactions decreases with successive infusions. Rituximab treatment is associated with blood and bone marrow toxicity manifested by neutropenia, leucopenia and infections. In addition, rituximab treatment is associated with flu-like symptoms and neurological problems.

For full details of side effects and contraindications, see the Summary of Product Characteristics available at http://emc.medicines.org.uk/.

CONTRAINDICATIONS

CONTRAINDICATIONS

For full details of contraindications, see the Summary of Product Characteristics available at http://emc.medicines.org.uk/.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by National Institute of Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 that requires local health boards and NHS trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.
- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the NICE Web site (www.nice.org.uk/TA137) (see also the "Availability of Companion Documents" field).
    - Costing report and costing template to estimate the savings and costs associated with implementation.
    - Audit support for monitoring local practice.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb. 29 p. (Technology appraisal guidance; no. 137).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Mar (revised 2008 Feb)

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor David Barnett, Professor of Clinical Pharmacology, University of Leicester; Dr David W Black, Director of Public Health, Derbyshire County PCT; Mr Brian Buckley, Chairman, Incontact; Dr Carol Campbell, Senior Lecturer, University of Teesside; Professor Mike Campbell, Professor of Medical Statistics, University of Sheffield; Professor David Chadwick, Professor of

Neurology, Liverpool University; Dr Peter Clarke, Consultant Medical Oncologist, Clatterbridge Centre for Oncology, Merseyside; Ms Jude Cohen-Phillips, Special Projects Consultant, UK Council for Psychotherapy; Dr Christine Davey, Senior Researcher, North Yorkshire Alliance R & D Unit; Dr Mike Davies, Consultant Physician, Manchester Royal Infirmary; Mr Richard Devereaux-Phillips, Public Affairs Manager, Medtronic; Dr Rachel A Elliott, Lord Trent Professor of Medicines and Health, University of Nottingham; Mrs Eleanor Grey, Lay member; Dr Catherine Jackson, Clinical Lecturer in Primary Care Medicine, Alyth Health Centre; Dr Peter Jackson, Clinical Pharmacologist, Sheffield Teaching Hospitals NHS Foundation Trust; Professor Peter Jones, Professor of Statistics and Dean, Faculty of Natural Sciences, Keele University; Ms Rachel Lewis, Practice Development Facilitator, Manchester PCT; Professor Jonathan Michaels, Professor of Vascular Surgery, University of Sheffield; Dr Eugene Milne, Deputy Medical Director, North East Strategic Health Authority; Dr Simon Mitchell, Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester; Dr Richard Alexander Nakielny, Consultant Radiologist, Royal Hallamshire Hospital, Sheffield; Dr Katherine Payne, Health Economics Research Fellow, University of Manchester; Mr Miles Scott, Chief Executive, Bradford Teaching Hospitals NHS Foundation Trust; Professor Andrew Stevens, Professor of Public Health, University of Birmingham and Chair of Appraisal Committee C; Dr Cathryn Thomas, GP and Associate Professor, University of Birmingham

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: National Institute for Health and Clinical Excellence (NICE). Guidance on the use of rituximab for recurrent or refractory Stage III or IV follicular non-Hodgkin's lymphoma. London (UK): National Institute for Health and Clinical Excellence (NICE); 2002 Mar. 24 p. (Technology appraisal guidance; no. 37).

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb. 2 p.

(Technology appraisal 137). Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

- Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma. Costing template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb. Various p. (Technology appraisal 137). Available in from the NICE Web site.
- Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 6 p. (Technology appraisal 137). Available in from the NICE Web site.
- Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma. Evidence review group report. NHS R&D Programme. Liverpool Reviews and Implementation Group. 2007 Aug 9. 87 p. Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1475. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 Feb. 4 p. (Technology appraisal 137).

Electronic copies: Available in Portable Document Format (PDF) from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the NHS Response Line 0870 1555 455. ref: N1476. 11 Strand, London, WC2N 5HR.

NGC STATUS

This NGC summary was completed by ECRI Institute on April 23, 2008. This summary was updated by ECRI Institute on October 8, 2008 following the U.S. Food and Drug Administration advisory on Rituxan (rituximab).

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